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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Joseph Loscalzo

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EXAMINER

SRIVASTAVA, KAILASH C

ART UNIT

PAPER NUMBER

1655

DATE MAILED: 07/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

DETAILED ACTION

1. Applicants' response filed 21 April 2006 to Office Action mailed 28 March 2006 is acknowledged and entered.
2. To ensure that all papers filed in a response remain together and for an expedient communication, especially during a telephone inquiry/interview to a response /amendment filed to an Office Action, Examiner will very much appreciate that in response to this Office Action, applicants label the header at each page of said response/amendment with U.S. Non-Provisional Application Serial number, U.S. Non-Provisional application filing date, Attorney's Docket number, First Applicant's name, Document Page number, Group Art Unit Number and Examiner's name. This practice immensely minimizes the papers lost during transaction/transmission and facilitates examination.

Claims Status

3. Claims 1-169 are pending

Restriction/Election

4. Applicants' election with traverse of Group I, Claims 1-25, filed 21 April 2006 to election requirement in Office Action mailed 28 March 2006 is acknowledged and entered. Despite the election being made with traverse, applicants have not presented any arguments traversing said election. Therefore, the restriction requirement is deemed proper and is made FINAL.
5. Accordingly, Claims 26-169 are withdrawn from further consideration as being directed to a non-elected invention. See 37 CFR §1.142(b) and MPEP § 821.03. Examiner suggests that the non-elected Claims 5 and 14-19 cited *supra* be canceled in response to this Office action to expedite further prosecution.
6. Claims 1-25 are examined on merits.

Priority

7. Applicants' claim for foreign priority under 35 U.S.C. § 119 (a-d) to PCT/US00/29582 filed on 10/26/ 2000 and PCT/US01/14245 filed on 05/02/ 2001 is acknowledged.
8. Applicants' claim for domestic priority under 35 U.S.C. § 119 (e) to Provisional U.S. Applications 60/162,230 and 60/179,020 filed on 10/29/ 1999 and 1/31/2000 respectively is acknowledged.

9. Applicants' Claim for domestic priority under 35 U.S.C. § 120 to Non-provisional U.S. application 10/415, 136 filed 04/25/2003 is also acknowledged.
10. Applicants' Claim for domestic priority under 35 U.S.C. § 121 to Non-provisional U.S. application 09/697,317 filed 10/27/2000, now U.S. Patent 6,635,273 is also acknowledged.

Information Disclosure Statement

11. Applicants' Information Disclosure Statements (i.e., IDSs) filed 28 January 2004, 02 September 2004 15 November 2004 and 05 July 2005 have been made of record and considered.

Objection to Information Disclosure Statement

12. Applicants' Information Disclosure Statement (i.e., IDS) filed 27 October 27, 2003 is objected to because the application number on forms 1449 labeled as Pages 2-5 accompanying said IDS is different than that of the instant application. However, to facilitate prosecution of this application, Examiner has considered said IDS. IN response to this Office Action Applicants, however, are required to refile the corrected 1449 with accurate application Number.

Claim Rejections - 35 U.S.C. § 103

13. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).
15. Claims 1-25 are rejected under 35 U.S.C. § 103 (a) as obvious over combined teachings from Birch et al (U.S. Patent 5,627,191) in view of Cohn (U.S. Patent 4,868, 179) and further in view of Chobanian et al (U. S. Patent 5,645,839).

Claims recite a sustained release formulation a small molecule antioxidant and isosorbide nitrate,

wherein the antioxidant is a hydralazine compound among others.

Birch et al. teach a composition comprising a hydralazine hydrochloride (Column 33, Lines 56-65; Column 34, Lines 1-3) in the treatment of cardiovascular disease, e.g., hypertension (Abstract). Birch et al., do not clearly teach the presence of isosorbide dinitrate in their composition. Further, the amount of hydralazine hydrochloride in their composition is not the same as is claimed in the instant invention. Cohn, however, teaches a composition comprising isosorbide dinitrate, digoxin and thiazide in addition to hydralazine hydrochloride (Column 2, Lines 26-60, Column 3, Lines 1-35). Note that hydralazine hydrochloride is a "small molecule" antioxidant. The hydralazine, but not the isosorbide nitrate concentration that Cohn teaches is in the same range as in instantly claimed invention. composition. Chobanian et al., teach a transdermal patch to administer their composition (Column 5, Lines 50-55) Note that a transdermal patch is a sustained release formulation and thus, intrinsically the combined teachings from Birch, Cohn and Chobanian read on the claimed invention because the prior art methods and composition teach treating the same disease applying the same formulation and steps.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify teachings from Birch et al. according to beneficial teachings from Cohn et al. and Chobanian et al. to obtain a sustained release formulation (i.e., transdermal patch) to treat the cardiovascular disease, because the teachings from prior art comprise a formulation having isosorbide dinitrate and a "small molecule" antioxidant, wherein said antioxidant is a hydralazine compound; because Birch et al. teach a composition comprising isosorbide dinitrate, Cohn et al. teach a composition comprising isosorbide dinitrate and hydralazine hydrochloride, wherein the concentration of hydralazine chloride in the same range as instantly claimed and Chobanian et al. teach a transdermal patch composition for the same purpose as is taught in Birch et al's composition. The concentration of isosorbide nitrate in the compositions disclosed in the prior art references is not the same as instantly claimed. However, the adjustment of particular conventional working conditions (e.g., the exact or range of quantities of each one of components in a composition) is deemed merely a matter of judicious selection and routine optimization of a result-effective parameter which is well within the purview of the skilled artisan.

Thus, at the time, the claimed invention was made, an artisan of ordinary skill would have been motivated to combine the teachings from Birch et al. according to beneficial teachings from Cohn et al. and Chobanian et al. to obtain a sustained release formulation comprising a "low molecule" antioxidant and isosorbide dinitrate and a method to treat a cardiovascular disease with the application of said formulation as discussed *supra*.

From the teachings of the references cited *supra*, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion


16. For reasons aforementioned, no Claims are allowed.


However, Claim 11 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. §112, 1st and 2nd paragraphs, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Terry McKelvey, can be reached on (571)-272-0775 Monday through Friday 8:00 A.M. to 4:30 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). Alternatively, status inquiries should be directed to the receptionist whose telephone number is (703) 308-0196.


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July 10, 2006